READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

[Pr]Folotyn®
pralatrexate injection

Read this carefully before you start taking **FOLOTYN®**. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **FOLOTYN®**.

What is FOLOTYN® used for?

- See the following boxed text.

For the following indication FOLOTYN® has been approved *with conditions* (NOC/c). This means it has passed Health Canada's review and can be bought and sold in Canada, but the manufacturer has agreed to complete more studies to make sure the drug works the way it should. For more information, talk to your healthcare professional.

FOLOTYN® treats a type of cancer called Peripheral T-cell Lymphoma (PTCL). It is used when the cancer does not go away, gets worse, or comes back after use of another cancer treatment.

What is a Notice of Compliance with Conditions (NOC/c)?

A Notice of Compliance with Conditions (NOC/c) is a type of approval to sell a drug in Canada.

Health Canada only gives an NOC/c to a drug that treats, prevents, or helps identify a serious or life-threatening illness. The drug must show promising proof that it works well, is of high quality, and is reasonably safe. Also, the drug must either respond to a serious medical need in Canada, or be much safer than existing treatments.

Drug makers must agree in writing to clearly state on the label that the drug was given an NOC/c, to complete more testing to make sure the drug works the way it should, to actively monitor the drug's performance after it has been sold, and to report their findings to Health Canada.

Serious Warnings and Precautions

Dermatologic Reactions (**severe skin reactions including Toxic Epidermal Necrolysis (TEN)):** These may happen to patients treated with FOLOTYN®. This can especially occur if you have lymphoma in or under your skin. It can start after the first dose. It tends to get worse over time. Patients with past or present skin disease are at higher risk. Problems with your skin and mucous membranes can become life-threatening and can lead to serious illness or death.

Bone Marrow Suppression (thrombocytopenia, neutropenia, or anemia): FOLOTYN® can affect your bone marrow's ability to make blood cells. It can cause you to have low blood cell counts.

Neutropenia is a low white blood cell count. It can occur with or without a fever. It can cause you to get infections. Serious illness or death can happen if an infection is not treated right away when white blood cell counts are very low.

Thrombocytopenia is low platelets in the blood. Platelets help with blood clotting.

Anemia is low red blood cell count.

Infections that can cause death such as pneumonia, sepsis, septic shock, and herpes zoster: when bacteria and their toxins circulate in the blood and start to damage organs.

Mucosal Inflammation: If left untreated, this may lead to death. Redness or sores on the mouth, lips, throat, digestive tract, and genitals. Discomfort or pain may occur a few days after starting on FOLOTYN®. Your doctor should tell you ways to reduce your risk of getting **Mucosal Inflammation**. They will tell you how to maintain nutrition and control the discomfort.

Tumour lysis Syndrome (TLS) is caused by cancer chemotherapy treatment. It is a complication due to the breakdown of cancer cells. It is serious and can lead to death. FOLOTYN® can cause the fast breakdown of certain types of cancer cells. When your body can't deal with so many dead cancer cells you can get TLS with changes to the normal electrolytes in your blood.

Potential harm to your unborn baby: If you are pregnant or plan to become pregnant. FOLOTYN® can harm your unborn baby. Females should avoid becoming pregnant while being treated with FOLOTYN®. Talk to your doctor about the best way to prevent pregnancy while taking FOLOTYN® and up to 8 weeks after ending treatment. Tell your doctor right away if you become pregnant while taking FOLOTYN®.

Pulmonary Toxicity (includes pneumonitis, respiratory failure, and acute respiratory distress syndrome): These lung related problems are serious and can cause death.

How does FOLOTYN® work?
FOLOTYN® is an anti-cancer agent (chemotherapy) prescription medicine. It belongs to a class of drugs called antifolates. FOLOTYN® is designed to help get pralatrexate into tumour cells and to keep it there. It upsets cancer cell repair and growth. It helps to slow or stop cancer cells from multiplying.

What are the ingredients in FOLOTYN®?
Medicinal ingredients: pralatrexate
Non-medicinal ingredients: sodium chloride, sodium hydroxide and if needed hydrochloric acid.

FOLOTYN® comes in the following dosage forms:
Solution for intravenous use:

- 20 mg of pralatrexate in 1 mL solution in a vial (20 mg / 1 mL)
- 40 mg of pralatrexate in 2 mL solution in a vial (40 mg / 2 mL)

Do not use FOLOTYN® if:
You are allergic to pralatrexate or to any of the ingredients in it.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take FOLOTYN®. Talk about any health conditions or problems you may have, including if you:
- have liver problems.
- have kidney problems. FOLOTYN® can cause kidney injury or failure.
- have any other medical conditions.
- are breast-feeding or plan to breast-feed. It is not known if FOLOTYN® passes into breast milk. You and your doctor should decide if you will take FOLOTYN® or breast-feed. You should not do both. Talk to your doctor about the best way to feed your baby while you are being treated with FOLOTYN®.

Other warnings you should know about:

Fever is one of the most common and earliest signs of infection. Follow your doctor's instructions about how often to take your temperature. This must especially be done the days right after treatment with FOLOTYN®.

Dehydration is the loss of too much fluid from the body often due to hot weather, vomiting, diarrhea, decrease blood pressure or lack of sweating. Follow your doctor's instructions for what to do to help prevent or treat it.

Sexual Health Male Patients
Before starting on FOLOTYN® you should know that it may affect your sexual function and fertility. If you want to have a child you may want to preserve some semen.

While on FOLOTYN®: It is not known if FOLOTYN® is present in semen. Avoid fathering a child during treatment. Use condoms with spermicide. Do this even after a vasectomy for sexual intercourse with female partners.

Driving, Hazardous Tasks and Using Machines: FOLOTYN® can cause fatigue. Before you do tasks which require special attention, wait until you know how you respond to it.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with FOLOTYN®:

- sulfamethoxazole / trimethoprim (Bactrim®, Septra®, Septra DS, Sulfatrim Pediatric, Sulfamethoprim, Sulfamethoprim-DS): a combination of two antibiotics used to treat different types of infections caused by bacteria.
- non-steroidal anti-inflammatory drugs (NSAIDs): a group of drugs that can reduce fever, pain and inflammation
- probenecid: sometimes given together with penicillin antibiotics to make them work better. It can be used to help your body pass uric acid out through your urine which lowers the levels of uric acid in your body.

How to take FOLOTYN®

To lower your chances of harmful side effects, it is important to take folic acid and vitamin B_{12} during your treatment with FOLOTYN®. Your doctor will give you specific instructions.

Folic Acid

- Take it by mouth
- Start 10 days before your first dose of FOLOTYN®.
- Do not take more or less than your doctor tells you to take.
- Continue to take it every day until your doctor tells you to stop.

Vitamin B_{12}

- Is an injection into your muscle (intramuscular)
- Start this before your first dose of FOLOTYN®
- Then get an injection every 8 to 10 weeks during treatment with FOLOTYN®.

How will I receive FOLOTYN®?

- FOLOTYN® is only given to patients who are under the care of a doctor who knows how to use anti-cancer drugs.
- FOLOTYN® comes in single use vials. Any unused drug left after injection must be discarded.
- The vials must be inspected before use. Be sure the liquid is clear yellow. Do NOT use it if the solution is hazy, has particles or solids, is discoloured or leaking.
- FOLOTYN® should NOT be diluted.
- A healthcare professional will give it to you over 3 to 5 minutes as an intravenous (IV) push. It will go from a syringe into the side port of an IV line. The IV line should contain 0.9% Sodium Chloride.
- FOLOTYN® is given in cycles,
    - One time each week for 6 weeks,
    - No treatment on the 7th week.
    - Treatment may continue as long as it is helpful to you.
    - It may be stopped if your disease gets worse or you have too many side effects.

Usual dose: 30 mg/m^2. If you have severe kidney disease, it is 15 mg/m^2.
The dose is based on your body size and on your medical condition. Your healthcare professional will regularly monitor your condition. Your dose may change depending on how well you tolerate FOLOTYN®. You may skip a dose or get a reduced dose.

Overdose:

In case of FOLOTYN® overdose, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:
You may be instructed by your doctor to miss a dose depending on how you tolerate FOLOTYN®.

What are possible side effects from using FOLOTYN®?
These are not all the possible side effects you may feel when taking FOLOTYN®. If you experience any side effects not listed here, contact your healthcare professional.

Side effects may include:
- nausea
- vomiting
- tiredness, fatigue
- constipation
- swelling
- cough
- nosebleed
- diarrhea

FOLOTYN® can cause abnormal blood test results. You should have blood tests before and during your treatment. These tests include checking how your liver and kidneys are working. FOLOTYN® can cause **Mucosal Inflammation**. Your doctor will decide when to perform physical assessments and do blood tests. They will interpret the results. Your doctor may change your dose or delay treatment based on the results of your blood tests and on your general condition.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Get immediate medical help
	Only if severe	In all cases	
COMMON			
Anemia: feeling weak, tired or short of breath, you look pale		✓	
Dehydration: thirst, headache, loss of appetite, feel tired and weak, lack of sweating. Decreased urine and blood pressure.		✓	

Pulmonary Toxicity (includes pneumonitis, respiratory failure, and acute respiratory distress syndrome) (non-infectious inflammation of the lungs): Shortness of breath, difficulty breathing, cough.			✓
Neutropenia: fever, chills, cough, shortness of breath, and pain or burning on urination			✓
Fever		✓	
Mucosal Inflammation: • Painful, red, shiny or swollen gums, tongue, mouth or throat sores. Blood in the mouth. Difficult or painful swallowing or talking, dry mouth, mild burning, or pain when eating food. Heartburn. • Passing mucus from your anus (back passage). Rectal bleeding. Blood in stools. • Vaginal itching, discharge odour, pain, infection and bleeding.		✓	
Infections such as pneumonia, sepsis, septic shock, and herpes zoster: Fever (high temperature), chills, and shivering. Fast heart rate and pulse (tachycardia), and rapid breathing.			✓
Severe skin reactions including Toxic Epidermal Necrolysis (TEN): Inflamed or flaky skin. Severe skin peeling, especially in mouth and eyes. Rash, sores, ulcers and blisters.			✓
Thrombocytopenia (low platelets that help blood clotting): unusual bleeding, such as nosebleeds, or bruising under your skin, fatigue and weakness.			✓

Tumour Lysis Syndrome (TLS): Nausea, shortness of breath, seizures, irregular heartbeat, vomiting, less urine produced, cloudy urine, tiredness or pain in joints.			✓
Kidney injury and kidney failure: less urine, urinate more often.		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store in carton until use. Protect from light. Refrigerate at 2-8ºC.

Unopened vial(s) are stable if stored in the original carton at room temperature for 72 hours. Any unopened vials left at room temperature for more than 72 hours should be discarded. Keep out of reach and sight of children.

If you want more information about FOLOTYN®:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (http://hc-sc.gc.ca/index-eng.php); the manufacturer's website www.servier.ca, or by calling 1-888-902-9700.

This leaflet was prepared by Servier Canada Inc.

® FOLOTYN is a registered trademark of Allos Therapeutics, Inc, used under license by Servier Canada Inc.

Last Revised on October 19, 2018